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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| EXAMINER | |
|---|---|
| LAM, ANN Y | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1641 | |

DATE MAILED: 10/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/807,345 | ARKHAMMAR ET AL. | |
| | Examiner | Art Unit | |
| | Ann Y. Lam | 1641 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *April 12, 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, line 2, recites the limitation "the cell". There is insufficient antecedent basis for this limitation in the claim.

Claims 12 and 13, line 2, recites the limitation "the fluorescence". There is insufficient antecedent basis for this limitation in the claim.

Regarding claim 14, line 4, and claim 15, lines 3 and 4, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 20, does not include a transitional phrase such as "comprising", and thus it is unclear what is included in the body of the claim.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

1. Claims 1-11, 15-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Zarling et al., 5,674,698.

Zarling et al. disclose a method for extracting quantitative information relating to an influence on redistribution of at least one component in a cell in mechanically intact or permeabilized living cells (see column 1, lines 12-30, and column 2, lines 53-61, and column 5, and column 5, lines 55-67), the method comprising recording variation in spatially distributed light emitted from a luminophore (see column 5, lines 55-67), the luminophore being present in the cells and being capable of being redistributed in a manner which is related with the degree of the influence and/or of being modulated by a component which is capable of being redistributed in a manner which is related to the degree of the influence, as a change in light intensity (see column 5, lines 55-67) wherein the illumination is provided by a laser which is scanned in a raster fashion over some or all of the spatial limitations being measured, the scanning taking place at a rate substantially faster than the measurement process such that the illumination appears to the measurement process to be continuous in time and spatially uniform over the region being measured, (see column 5, line 54 – column 6, line 3, and column 6, 54-67, and column 7, lines 11-16, and column 7, lines 44-64.)

As to claim 2, the quantitative information which is indicative of the degree of the cellular response to the influence or the result of the influence on the subcellular component is extracted from the recorded variation according to a predetermined calibration based on responses or results, recorded in the same manner, to known degrees of a relevant specific influence, (see column 5, lines 54-67, and column 6, 54-67, and column 7, lines 11-16, and column 7, lines 44-64.)

As to claim 3, the influence comprises contact between the mechanically intact or permeabilised living cells and a chemical substance and/or incubation of the cells with a chemical substance (see column 5, lines 9-14 and see column 5, lines 54-67, and column 6, 54-67, and column 7, lines 11-16, and column 7, lines 44-64.)

As to claim 4, the cells comprise a group of cells contained within a spatial limitation type (see column 49, lines 10-32.)

As to claim 5, the cells comprises multiple groups of cells contained within multiple spatial limitations As to claim 6, the spatial limitations are spatial limitations arranged in one or more arrays on a common carrier type (see column 49, lines 10-32.)

As to claim 7, the spatial limitations are wells in a plate of micro-titer type (see column 49, lines 10-32.)

As to claim 8, the redistribution results in quenching of fluorescence, the quenching being measure as a decrease in the intensity of the fluorescence, (see column 5, line 55 – column 6, line 3.)

As to claim 9, the redistribution results in energy transfer, the energy transfer being measure as a change in the intensity of the luminescence (see column 5, line 55 – column 6, line 3.)

As to claim 10, the intensity of the light being recorded is a function of the fluorescence lifetime, polarization, wavelength shift, or other property which is modulated as a result of the underlying cellular response, (see column 5, line 55 – column 6, line 3.)

As to claim 11, the light to be measured passes through a filter which selects the desired component of the light to be measured and rejects other components (see column 6, line 3.)

As to claim 15, the cells are selected from the group consisting of fungal cells, invertebrate cells, vertebrate cells (see column 5, line 13.)

As to claim 12, the fluorescence comes from a fluorophore encoded by and expressed fro a nucleotide sequence harboured in the cells (see column 28, line 67 – column 29, lines 17.)

As to claim 16, the living cells are mammalian cells which, during the time period over which the influence is observed, are incubated at a temperature of 30 degrees Celsius or above (see column 21, lines 59-67.)

As to claim 17, the method is used as a screening program (see column 7, lines 56-64.)

As to claim 20, a set of date obtained by the above method is disclosed (see column 7, lines 56-64.)

As to claim 18, Zarling et al. disclose use of fluorescence microscopy wherein the method is for screening program for the identification of a biologically active substance that directly or indirectly affects an intracellular signaling pathway and is potentially useful as a medicament, wherein the result of the individual measurement of each substance being screened which indicates its potential biological activity is based on measurement of the redistribution of spatially resolved luminescence in living cells and which undergoes a change in distribution upon activation of an intracellular signaling pathway (see column 7, lines 56-64.)

As to claim 19, the method is a screening program for the identification of a biologically toxic substance that exerts its toxic effect by interfering with an intracellular signaling pathway, wherein the result of the individual measurement of each substance being screened which indicates its potential biologically toxic activity is based on measurement of the redistribution of said fluorescent probe in living cells and which undergoes a change in distribution upon activation of an intracellular signaling pathway (see column 7, lines 56-64.)

**2.** Claims 1-11, 15-17 and 20 are rejected under 35 U.S.C. 102(e) as being anticipated by Baer, 6,259,104.

Baer discloses a method for extracting quantitative information relating to an influence on redistribution of at least one component in a cell in mechanically intact or permeabilized living cells (see column 1, lines 25 and 37, and column 2, lines 52-55), the method comprising recording variation in spatially distributed light emitted from a

luminophore (see column 10, lines 47-54), the luminophore being present in the cells and being capable of being redistributed in a manner which is related with the degree of the influence and/or of being modulated by a component which is capable of being redistributed in a manner which is related to the degree of the influence, as a change in light intensity (see column 7, lines 1-5) wherein the illumination is provided by a laser which is scanned in a raster fashion over some or all of the spatial limitations being measured, the scanning taking place at a rate substantially faster than the measurement process such that the illumination appears to the measurement process to be continuous in time and spatially uniform over the region being measured, (see column 22, lines 12-17.)

As to claim 2, the quantitative information which is indicative of the degree of the cellular response to the influence or the result of the influence on the subcellular component is extracted from the recorded variation according to a predetermined calibration based on responses or results, recorded in the same manner, to known degrees of a relevant specific influence, (see column 1, lines 25 and 27, and column 2, lines 52-54, and column 7, lines 1-5).

As to claim 3, the influence comprises contact between the mechanically intact or permeabilised living cells and a chemical substance and/or incubation of the cells with a chemical substance (see column 1, lines 25 and 37, and column 2, lines 52-54, and column 8, line 30.)

As to claim 4, the cells comprise a group of cells contained within a spatial limitation (see column 1, lines 25 and 37, and column 2, lines 52-54.)

As to claim 5, the cells comprises multiple groups of cells contained within multiple spatial limitations (see column 1, lines 25 and 37, and column 2, lines 52-54.).

As to claim 6, the spatial limitations are spatial limitations arranged in one or more arrays on a common carrier (see column 1, lines 25 and 37, and column 2, lines 52-54.).

As to claim 7, the spatial limitations are wells in a plate of micro-titer type (see column 1, lines 25 and 37, and column 2, lines 52-54.)

As to claim 8, the redistribution results in quenching of fluorescence, the quenching being measure as a decrease in the intensity of the fluorescence, (see column 3, line 3).

As to claim 9, the redistribution results in energy transfer, the energy transfer being measure as a change in the intensity of the luminescence (see column 3, line 3.)

As to claim 10, the intensity of the light being recorded is a function of the fluorescence lifetime, polarization, wavelength shift, or other property which is modulated as a result of the underlying cellular response, (see column 3, lines 2-3.)

As to claim 11, the light to be measured passes through a filter which selects the desired component of the light to be measured and rejects other components (see column 21, lines 35-36.)

As to claim 15, the cells are selected from the group consisting of fungal cells, invertebrate cells, vertebrate cells As to claim 12, the fluorescence comes from a fluorophore encoded by and expressed fro a nucleotide sequence harboured in the cells (see column 1, lines 25 and 27, and column 2, lines 52-54, and column 7, lines 1-5).

As to claim 16, the living cells are mammalian cells which, during the time period over which the influence is observed, are incubated at a temperature of 30 degrees Celsius or above (see column 1, lines 25 and 27, and column 2, lines 52-54, and column 7, lines 1-5).

As to claim 17, the method is used as a screening program (see column 1, lines 25 and 27, and column 2, lines 52-54, and column 7, lines 1-5).

As to claim 20, a set of date obtained by the above method is disclosed (see column 1, lines 25 and 27, and column 2, lines 52-54, and column 7, lines 1-5).

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

**3.** Claims 18 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baer, 6,259,104, in view of Bawendi et al., 6,306,610.

Baer discloses the invention substantially as claimed. Baer discloses that the invention is useful in fluorescence microscopy, (see column 1, lines 24 and 37, and column 2, lines 52-54.

However, Baer does not specifically disclose use of the invention in fluorescence microscopy as claimed by Applicant.

Bawendi et al disclose use of fluorescence microscopy as claimed by Applicant.

As to claim 18, Bawendi et al. disclose use of fluorescence microscopy wherein the method is for screening program for the identification of a biologically active substance that directly or indirectly affects an intracellular signaling pathway and is potentially useful as a medicament, wherein the result of the individual measurement of each substance being screened which indicates its potential biological activity is based on measurement of the redistribution of spatially resolved luminescence in living cells and which undergoes a change in distribution upon activation of an intracellular signaling pathway (see column 1, lines 42-44, and column 2, lines 2-19, and column 20, lines 51-65.)

As to claim 19, the method is a screening program for the identification of a biologically toxic substance that exerts its toxic effect by interfering with an intracellular signaling pathway, wherein the result of the individual measurement of each substance being screened which indicates its potential biologically toxic activity is based on measurement of the redistribution of said fluorescent probe in living cells and which undergoes a change in distribution upon activation of an intracellular signaling pathway (see column 1, lines 42-44, and column 2, lines 2-19, and column 20, lines 51-65.)

Since Baer teaches that the invention is applied specifically to the field of fluorescence microscopy (see column 2, lines 52-54), it would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the Baer

invention for the identification of biologically active substance as taught by Bawendi et al., as known identification methods in the field of fluorescence microscopy.

**4.** Claims 12-14 rejected under 35 U.S.C. 103(a) as being unpatentable over Baer, 6,259,104, in view of Cormack et al., 6,090,919.

Baer discloses the invention substantially as claimed (see above), except for the specific luminophores claimed.

Cormack et al. fluorescence labeling as a useful tool for marking a protein or cell of interest, in vivo studies, see column 1, lines 22-27, and that a marker that does not require any exogenous cofactor or substrate is the green fluorescent protein (GFP), see column 1, lines 22-40.

As to claim 12, Cormack et al. disclose that the fluorescence comes from a fluorophore encoded by and expressed from a nucleotide sequence harboured in the cells, (see column 1, lines 38-39, column 8, lines 22-24.)

As to claim 13, the fluorescence comes from a luminescent polypeptide, such as GFP, (see column 1, lines 38-39, column 8, lines 22-24.).

As to claim 14, the luminescent polypeptide could be a GFP selected from the claimed green fluorescent proteins, (see column 1, lines 38-39, column 8, lines 22-24.)

Since Cormack et al. teaches GFP as an alternative to a fluorophore derivative that is inserted into cells, the GFP having the benefit of not requiring any exogenous cofactor or substrate, see column 1, lines 38-39, it would have been obvious to use the

GFP as the luminophore in the Baer invention, as a substitute luminophore that has the benefit of not requiring any exogenous cofactor or substrate.

**5.** Claims 12-14 rejected under 35 U.S.C. 103(a) as being unpatentable over Zarling, 5,674,698, in view of Cormack et al., 6,090,919.

Zarling discloses the invention substantially as claimed (see above), except for the specific luminophores claimed.

Cormack et al. fluorescence labeling as a useful tool for marking a protein or cell of interest, in vivo studies, see column 1, lines 22-27, and that a marker that does not require any exogenous cofactor or substrate is the green fluorescent protein (GFP), see column 1, lines 22-40.

As to claim 12, Cormack et al. disclose that the fluorescence comes from a fluorophore encoded by and expressed from a nucleotide sequence harboured in the cells, (see column 1, lines 38-39, column 8, lines 22-24.)

As to claim 13, the fluorescence comes from a luminescent polypeptide, such as GFP, (see column 1, lines 38-39, column 8, lines 22-24.).

As to claim 14, the luminescent polypeptide could be a GFP selected from the claimed green fluorescent proteins, (see column 1, lines 38-39, column 8, lines 22-24.)

Since Cormack et al. teaches GFP as an alternative to a fluorophore derivative that is inserted into cells, the GFP having the benefit of not requiring any exogenous cofactor or substrate, see column 1, lines 38-39, it would have been obvious to use the

GFP as the luminophore in the Zarling invention, as a substitute luminophore that has the benefit of not requiring any exogenous cofactor or substrate.

***Conclusion***

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Myers, 5,108,179, discloses fluorophore stained nucleic acid fragments.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ann Y. Lam whose telephone number is (703) 306-5560. The examiner can normally be reached on M-Sat 11-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (703)305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703)308-0196.

A.L.

BAO-THUY L. NGUYEN
PRIMARY EXAMINER
9/30/03